

IN THE CLAIMS:

1. (Currently amended) A method for producing a recombinant retroviral particle, said particle comprising an RNA sequence ~~which encodes~~ encoding an SDI-1 polypeptide, or a functional analogue or a functional fragment thereof, ~~of the RNA sequence which encodes a polypeptide with SDI-1 activity of inhibiting cell proliferation,~~ the method comprising stably transfecting an isolated producer cell line with a retroviral vector comprising in 5' to 3' order:

- (a) a 5' LTR region of the structure U3-R-U5;
- (b) ~~one or more sequences selected from an SDI-1 coding and noncoding sequence[[s]];~~ and
- (c) a 3' LTR region comprising a completely or partially deleted U3 region, wherein into said deleted U3 region ~~is replaced by~~ has been cloned a polylinker sequence ~~containing~~ into which a regulatory element or a promoter has been inserted, followed by the U5 and R region,

~~characterized in that at least one of the coding sequences is a sequence encoding SDI-1, a functional analogue thereof, or a functional fragment thereof, said SDI-1 sequence encoding a polypeptide with SDI-1 activity of inhibiting cell proliferation and being under transcriptional control of said regulatory element or promoter,~~

wherein:

- (i) said SDI-1 polypeptide or functional fragment thereof inhibits cell proliferation;
- (ii) after infection of a target cell by said recombinant retroviral particle, said U3 of said 5' long terminal repeat region is replaced by said completely or partially deleted U3 region and said regulatory element or promoter, resulting in said SDI-1 coding sequence becoming operatively linked to said regulatory element or promoter and said regulatory element or promoter regulating expression of said SDI-1 coding sequence in said target cell; and

- (iii) said isolated producer cell line additionally harboring comprises at least one DNA construct encoding for a protein[[s]] required for said retroviral vector to be packaged.
2. (Previously presented) The method of Claim 1 wherein the retroviral vector comprises a DNA sequence encoding SDI-1.
3. (Currently amended) The method of Claim ~~[[2]]~~ 1, wherein the ~~DNA sequence codes for functional fragment~~ comprises amino acids 1 to 71 of human SDI-1.
4. (Currently amended) The method of Claim ~~[[2]]~~ 1, wherein the ~~DNA sequence codes for functional fragment~~ comprises amino acids 42 to 58 of human SDI-1.
5. (Withdrawn) A retroviral vector according to Claim 1 carrying a DNA sequence which is antisense to the SDI-1 gene.
6. (Withdrawn) A retroviral vector according to Claim 1 wherein the antisense SDI-1 DNA sequence is 10 to 30, preferably 15 to 24 nucleotides long and prepared according to the nucleotide sequence of the SDI-1 gene.
7. (Withdrawn) A retroviral vector according to Claim 6 wherein the antisense SDI-1 DNA sequence is antisense to nucleotides 75 to 93 of the DNA sequence encoding SDI-1.
8. Canceled.
9. (Currently amended) The method of Claim ~~[[1]]~~ 2, wherein the DNA sequence encoding an SDI-1 polypeptide, ~~a functional analogue~~, or a functional fragment thereof is under transcriptional control of a regulatory element selected from the group consisting of a target cell specific regulatory element, or a target cell specific promoter, or and an X-ray inducible promoter.
10. (Currently amended) The method of Claim 9 wherein the ~~target cell specific~~ regulatory element is selected from the group consisting of a Whey Acidic Protein (WAP) regulatory element and a mouse mammary tumor virus (MMTV) regulatory element[[s]].
11. (Previously presented) The method of Claim 10 wherein the retroviral vector is pLXS-SDI1.

12. (Withdrawn) A retroviral vector according to Claim 10 which is pLX125.IDS.

13. (Currently amended) An isolated producer cell line stably transfected with a retroviral vector comprising in 5' to 3' order:

- (a) a 5' LTR region of the structure U3-R-U5;
- (b) ~~one or more sequences selected from a coding sequence[[s]] encoding~~
an SDI-1 polypeptide or a functional fragment thereof; and
- (c) a 3' LTR region comprising a completely or partially deleted U3 region, wherein into said deleted U3 region ~~is replaced by~~ has been cloned a polylinker sequence ~~containing~~ into which a regulatory element or a promoter has been inserted, followed by the U5 and R region,

~~characterized in that at least one of the coding sequences is a sequence encoding SDI-1, a functional analogue thereof, or a functional fragment thereof, said SDI-1 sequence encoding a polypeptide with SDI-1 activity of inhibiting cell proliferation and being under transcriptional control of said regulatory element or promoter,~~

wherein:

- (i) said SDI-1 polypeptide or functional fragment thereof inhibits cell proliferation;
- (ii) after infection of a target cell by said recombinant retroviral particle, said U3 of said 5' long terminal repeat region is replaced by said completely or partially deleted U3 region and said regulatory element or promoter, resulting in said SDI-1 coding sequence becoming operatively linked to said regulatory element or promoter and said regulatory element or promoter regulating expression of said SDI-1 coding sequence in said target cell; and
- (iii) said isolated producer cell line additionally harboring comprises at least one DNA construct encoding for the a protein[[s]] required for said retroviral vector to be packaged.

14. (Currently amended) The isolated producer cell line of Claim 13, wherein the isolated producer cells line which is a of human cell line origin.

15. (Currently amended) A capsule ~~which encapsulates~~ comprising:

- (a) an isolated producer cell line stably transfected with a retroviral vector comprising a DNA sequence encoding an SDI-1 polypeptide, ~~a functional analogue thereof~~, or a functional fragment thereof, wherein the SDI-1 ~~or functional fragment or functional analogue thereof~~ polypeptide or functional fragment thereof inhibits cell proliferation, and said isolated producer cell line ~~additionally harboring~~ comprises at least one DNA construct encoding for the a protein[[s]] required for said retroviral vector to be packaged; and, ~~said capsule comprising~~
- (b) a porous capsule wall being that is permeable to the retroviral particles produced by said isolated producer cell line.

16. (Previously presented) The capsule of Claim 15 wherein said porous capsule wall comprises a polyelectrolyte complex formed from counter charged polyelectrolytes.

17. Canceled.

18. (Withdrawn) A recombinant retroviral particle produced by culturing a packaging cell line according to Claim 13 harbouring a retroviral vector carrying an antisense SDI-1 DNA sequence under suitable conditions optionally followed by isolation of the recombinant retroviral particle produced.

19. (Currently amended) A pharmaceutical composition comprising the isolated producer cell line of Claim 13 and a pharmaceutically acceptable carrier or diluent.

20. (Previously presented) A pharmaceutical composition comprising the capsule of Claim 15 and a pharmaceutically acceptable carrier or diluent.

21. (Currently amended) A method of treating a tumor or restenosis in an individual having a tumor or restenosis, comprising administering to the individual at ~~the a~~ a site of the tumor or the restenosis the capsule of Claim 15.

22. Canceled.

23. (Previously presented) The method according to Claim 21 wherein the tumor is a breast tumor.

24. (Withdrawn) The use of a retroviral particle according to Claim 18 for the preparation of a medicament for the treatment of a disorder or disease responsive to the proliferative activity of antisense SDI-1 DNA sequences.

25. (Withdrawn) The use according to Claim 24 for the preparation of a medicament for the treatment of cancer.

26. (Currently amended) A method for introducing a DNA sequence[[s]] encoding an SDI-1 polypeptide, ~~a functional analogue~~, or a functional fragment thereof, into a human cell[[s]] *in vitro*, the method comprising infecting the human cell[[s]] with a retroviral particle produced by the isolated producer cell line of Claim 13.

27. (Currently amended) A method for ~~the treatment of~~ treating a subject having a tumor or restenosis, the method comprising administering to ~~a living animal body, including a human, in need thereof~~ the subject a therapeutically effective amount of a recombinant retroviral particle produced by the isolated producer cell line of Claim 13 at ~~the~~ a site of the tumor or restenosis.

28. Canceled.

29. (Withdrawn) A method for the treatment of a disorder or disease responsive to the proliferative activity of antisense SDI-1 DNA sequences comprising administering to a living animal body, including a human, in need thereof a therapeutically effective amount of a retroviral particle according to Claim 18.

30. (Withdrawn) A method according to Claim 29 wherein the disorder or disease is cancer, and the administration of the retroviral particle is combined with irradiation.

31. (Currently amended) The method according to Claim 27 wherein the ~~recombinant retroviral particle is administered~~ administering is by as an injection of the recombinant retroviral particle into the living animal body, including a human, at the a site of the tumor or restenosis.

32. Canceled.

33. (Currently amended) A method for producing a recombinant retroviral particle, said particle comprising an RNA sequence ~~which encodes~~ encoding an SDI-1 polypeptide, ~~wherein the SDI-1 inhibits cell proliferation, the method~~ comprising stably transfecting an isolated producer cell line with a retroviral vector comprising in 5' to 3' order:

- (a) a 5' LTR region of the structure U3-R-U5;
- (b) ~~one or more sequences selected from a coding sequence encoding the SDI-1 polypeptide; and noncoding sequences;~~ and
- (c) a 3' LTR region comprising a completely or partially deleted U3 region, wherein into said deleted U3 region ~~is replaced by~~ has been cloned a polylinker sequence ~~containing~~ into which a regulatory element or a promoter has been inserted, followed by the U5 and R region,

~~characterized in that at least one of the coding sequences is a sequence encoding SDI-1, said SDI-1 sequence encoding a polypeptide with SDI-1 activity of inhibiting cell proliferation and being under transcriptional control of said regulatory element or promoter,~~

wherein:

- (i) said SDI-1 polypeptide inhibits cell proliferation;
- (ii) after infection of a target cell by said recombinant retroviral particle, said U3 of said 5' long terminal repeat region is replaced by said completely or partially deleted U3 region and said regulatory element or promoter, resulting in said SDI-1 coding sequence becoming operatively linked to said regulatory element or promoter and said regulatory element or promoter regulating expression of said SDI-1 coding sequence in said target cell; and
- (iii) said isolated producer cell line additionally harboring comprises at least one DNA construct encoding for a protein[[s]] required for said retroviral vector to be packaged.

34. Canceled.

35. Canceled.

36. (Currently amended) The method of Claim 33 wherein the ~~DNA sequence encoding SDI-1 is under transcriptional control of a~~ regulatory element or promoter is selected from the group consisting of a target cell specific regulatory element, or a target cell specific promoter, or and an X-ray inducible promoter.

37. (Currently amended) The method of Claim 36 wherein the ~~target cell specific~~ regulatory element is selected from the group consisting of a Whey Acidic Protein (WAP) regulatory element and a mouse mammary tumor virus (MMTV) regulatory element[[s]].

38. (Previously presented) The method of Claim 37 wherein the retroviral vector is pLXS-SDI1.

39. (Currently amended) An isolated producer cell line stably transfected with a retroviral vector comprising in 5' to 3' order:

- (a) a 5' LTR region of the structure U3-R-U5;
- (b) ~~one or more sequences selected from a sequence encoding an SDI-1 polypeptide and noncoding sequences;~~ and
- (c) a 3' LTR region comprising a completely or partially deleted U3 region, wherein into said deleted U3 region ~~is replaced by~~ has been cloned a polylinker sequence ~~containing~~ into which a regulatory element of a promoter has been inserted, followed by the U5 and R region,

~~characterized in that at least one of the coding sequences is a sequence encoding SDI-1, a functional analogue thereof, or a functional fragment thereof, said SDI-1 sequence encoding a polypeptide with SDI-1 activity of inhibiting cell proliferation and being under transcriptional control of said regulatory element or promoter,~~

wherein:

- (i) said SDI-1 polypeptide inhibits cell proliferation;
- (ii) after infection of a target cell by said recombinant retroviral particle, said U3 of said 5' long terminal repeat region is replaced

by said completely or partially deleted U3 region and said regulatory element or promoter, resulting in said SDI-1 coding sequence becoming operatively linked to said regulatory element or promoter and said regulatory element or promoter regulating expression of said SDI-1 coding sequence in said target cell; and

- (iii) said isolated producer cell line additionally harboring comprises at least one DNA construct encoding for the a protein[[s]] required for said retroviral vector to be packaged.

40. (Currently amended) The isolated producer cell line of Claim 39, wherein the isolated producer cell line which is a of human cell line origin.

41. (Currently amended) A capsule ~~which encapsulates~~ comprising:

- (a) an the isolated producer cell line of Claim 39 stably transfected with a retroviral vector comprising a DNA sequence encoding SDI-1, wherein the SDI-1 inhibits cell proliferation said producer cell line additionally harboring at least one DNA construct coding for the proteins required for said retroviral vector to be packaged, said capsule comprising ; and
- (b) a porous capsule wall being that is permeable to the retroviral particles produced by said isolated producer cell line.

42. (Previously presented) The capsule of Claim 41 wherein said porous capsule wall comprises a polyelectrolyte complex formed from counter charged polyelectrolytes.

43. (Currently amended) A method for introducing a DNA sequence[[s]] encoding an SDI-1 polypeptide into a human cell[[s]] in vitro, the method comprising infecting the human cell[[s]] with a retroviral particle produced by the isolated producer cell line of Claim 39.

44. (Currently amended) A method for producing a recombinant retroviral particle, said particle comprising an RNA sequence ~~which codes for encoding a polypeptide comprising~~ amino acids 1 to 71 of human SDI-1 ~~and inhibits cell proliferation,~~ the method comprising stably transfecting an isolated producer cell line

with a retroviral ~~sequence~~ vector comprising a DNA sequence which encodes SDI-1 the polypeptide, wherein:

- (i) the SDI-1 polypeptide inhibits cell proliferation[[],] ; and
- (ii) said producer cell ~~additionally harboring~~ comprises at least one DNA construct encoding for a protein[[s]] required for said retroviral vector to be packaged.

45. (Currently amended) An isolated producer cell line stably transfected with a retroviral vector comprising in 5' to 3' order:

- (a) a 5' LTR region of the structure U3-R-U5;
- (b) ~~one or more sequences selected from a sequence encoding a~~ polypeptide comprising amino acids 1-71 of human SDI-1 and noncoding sequences; and
- (c) a 3' LTR region comprising a completely or partially deleted U3 region, wherein into said deleted U3 region ~~is replaced by~~ has been cloned a polylinker sequence ~~containing into which~~ a regulatory element or a promoter has been inserted, followed by the U5 and R region,

~~characterized in that at least one of the coding sequences is a sequence encoding amino acids 1-71 of SDI-1, said SDI-1 sequence encoding a polypeptide with SDI-1 activity of inhibiting cell proliferation and being under transcriptional control of said regulatory element or promoter,~~

wherein:

- (i) said polypeptide inhibits cell proliferation;
- (ii) after infection of a target cell by said recombinant retroviral particle, said U3 of said 5' long terminal repeat region is replaced by said completely or partially deleted U3 region and said regulatory element or promoter, resulting in said SDI-1 coding sequence becoming operatively linked to said regulatory element or promoter and said regulatory element or promoter regulating expression of said SDI-1 coding sequence in said target cell; and

- (iii) said isolated producer cell line ~~additionally harboring~~ comprises at least one DNA construct encoding ~~for the~~ a protein[[s]] required for said retroviral vector to be packaged.

46. (Currently amended) A capsule ~~which encapsulates~~ comprising:

- (a) the isolated producer cell line of Claim ~~[[44,]]~~ 45; and
(b) ~~said capsule comprising a porous capsule wall being~~ that is permeable to ~~the~~ retroviral particles produced by said isolated producer cell line.

47. (Previously presented) The capsule of Claim 46 wherein said porous capsule wall comprises a polyelectrolyte complex formed from counter charged polyelectrolytes.

48. (Currently amended) A method for introducing a DNA sequence[[s]] encoding a polypeptide comprising amino acids 1-71 of human SDI-1 into a human cell[[s]] in vitro, the method comprising infecting the human cell[[s]] with a retroviral particle produced by the isolated producer cell line of Claim 45.

49. (Currently amended) A method for producing a recombinant retroviral particle, said particle comprising an RNA sequence ~~which codes for~~ encoding a polypeptide comprising amino acids 42 to 58 of human SDI-1 ~~and inhibits cell proliferation~~, the method comprising stably transfecting an isolated producer cell line with a retroviral vector comprising a DNA sequence which encodes the polypeptide SDI-1, wherein:

- (i) the SDI-1 polypeptide inhibits cell proliferation[[,]] ; and
(ii) said producer cell ~~additionally harboring~~ comprises at least one DNA construct encoding ~~for~~ a protein[[s]] required for said retroviral vector to be packaged.

50. (Currently amended) An isolated producer cell line stably transfected with a retroviral vector comprising in 5' to 3' order:

- (a) a 5' LTR region of the structure U3-R-U5;

(b) ~~one or more sequences selected from a sequence encoding a polypeptide comprising amino acids 42-58 of human SDI-1 and noncoding sequences; and~~

(c) a 3' LTR region comprising a completely or partially deleted U3 region, wherein into said deleted U3 region ~~is replaced by~~ has been cloned a polylinker sequence ~~containing~~ into which a regulatory element or promoter has been inserted, followed by the U5 and R region,

~~characterized in that at least one of the coding sequences is a sequence encoding amino acids 42-58 of SDI-1, said SDI-1 sequence encoding a polypeptide with SDI-1 activity in inhibiting cell proliferation and being under transcriptional control of said regulatory element or promoter,~~

wherein:

- (i) said polypeptide inhibits cell proliferation;
- (ii) after infection of a target cell by said recombinant retroviral particle, said U3 of said 5' long terminal repeat region is replaced by said completely or partially deleted U3 region and said regulatory element or promoter, resulting in said SDI-1 coding sequence becoming operatively linked to said regulatory element or promoter and said regulatory element or promoter regulating expression of said SDI-1 coding sequence in said target cell; and
- (iii) said isolated producer cell line additionally harboring comprises at least one DNA construct encoding for the a protein[[s]] required for said retroviral vector to be packaged.

51. (Currently amended) A capsule ~~which encapsulates~~ comprising:

- (a) the isolated producer cell line of Claim 50; and
- (b) , said capsule comprising a porous capsule wall being that is permeable to the retroviral particles produced by said isolated producer cell line.

52. (Previously presented) The capsule of Claim 51 wherein said porous capsule wall comprises a polyelectrolyte complex formed from counter charged polyelectrolytes.

53. (Currently amended) A method for introducing a DNA sequence encoding a polypeptide comprising amino acids 42-58 of human SDI-1 into a human cell *in vitro*, the method comprising infecting the human cell with a retroviral particle produced by the isolated producer cell line of Claim 50.

54. (Previously presented) A recombinant retroviral particle produced by the method of Claim 1.

55. (Previously presented) A pharmaceutical composition comprising the retroviral particle of Claim 54 and a pharmaceutically acceptable carrier or diluent.

56. Canceled.

57. Canceled.

58. (Currently amended) A pharmaceutical composition comprising the capsule of Claim ~~[[56]]~~ 51 and a pharmaceutically acceptable carrier or diluent.

59. (Currently amended) A method of treating a tumor or restenosis in an individual having a tumor or restenosis, comprising administering to the individual the capsule of Claim ~~[[56]]~~ 51 at ~~the~~ a site of the tumor or the restenosis.

60. Canceled.

61. (Previously presented) The method according to Claim 59 wherein the tumor is a breast tumor.

62. Canceled.

63. (Currently amended) A method for the treatment of a subject having a tumor or restenosis, the method comprising implanting into the subject at a site of the tumor a capsule ~~having a core, wherein the core comprises~~ comprising:

(a) a plurality of packaging cells harbouring comprising:

(a) (i) a retroviral vector carrying comprising a DNA sequence encoding an SDI-1 polypeptide, a functional analogue, or a functional fragment thereof or an antisense SDI-1 DNA sequence; and

(b) (ii) at least one DNA construct encoding for the a protein[[s]] required for said retroviral vector to be packaged; and

(b) ~~and wherein a porous capsule wall surrounds said core, said porous capsule wall being that is permeable to retroviral particles produced by the packaging cells, into the living animal body, including a human, at the site of the tumor.~~

64. Canceled.